CHEMISTRY
A EUROPEAN JOURNAL

DOI: 10.1002/chem.201100729

S_N1-Type Reactions in the Presence of Water: Indium(III)-Promoted Highly Enantioselective Organocatalytic Propargylation of Aldehydes

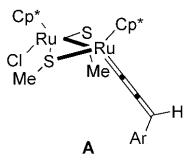
Riccardo Sinisi, Maria Victoria Vita, Andrea Gualandi, Enrico Emer, and Pier Giorgio Cozzi*[a]

Dedicated to Professor Carmen Najera on the occasion of her 60th birthday

Organocatalysis has received considerable attention in the past 10 years[1] and is becoming an exciting area of research, particularly as organocatalytic transformations are now being considered in the design of syntheses of complex natural products[2] and drugs.[3] Most of the organocatalytic reactions involve two basic activation routes: enamine catalysis[4] and iminium catalysis.[5] More recently, the combination of oxidants in the presence of organocatalysts[6] and the use of photoredox properties of metal complexes have been reported,[7] thus opening up new frontiers in the field of organocatalysis.

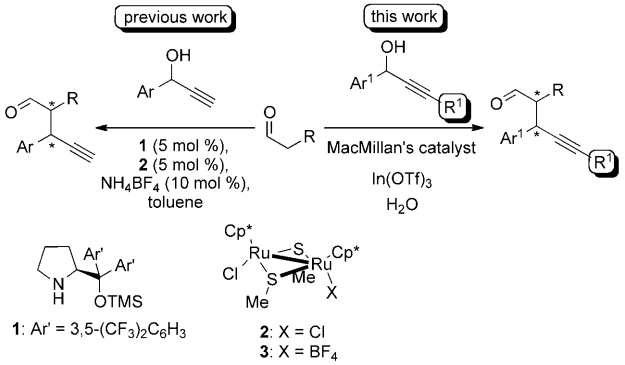
Recently, the concept of combining organocatalysis with organotransition metal complexes has led to exciting strategies for the development of innovative transformations.[8] In particular, Nishibayashi described a highly enantioselective propargylation of aldehydes by combining the Hayashi–Jørgensen organocatalyst derivative **1** with a ruthenium complex (Scheme 1).[9] The methanothiolated-bridged diruthenium complex $[\{Cp^*RuCl(\mu_2\text{-}SMe)\}_2]$ ($Cp^* = \eta^5C_5Me_5$) **2** activated with NH_4BF_4 formed a cationic ruthenium complex **3** which was able to transform the alkynyl alcohol through a stabilized formal propargylic carbocation,[10] which reacts with the chiral enamine through an S_N1 mechanism.[11]

However, no reaction occurred when propargylic alcohols with an internal alkyne moiety were used under identical reaction conditions. This observation, reported by Nishibayashi clearly indicates that the formation of the ruthenium–allenylidene **A** complex is crucial for this kind of reaction.[12]



A

Although the enantiomeric excesses (*ee*) were excellent for the major *syn* stereoisomer, long reaction times (40–120 h) were necessary to accomplish the transformation using toluene as the reaction solvent. On the other hand, propargylic alcohols can be activated towards S_N1 type reactions with nucleophiles using a variety of Lewis acids or Brønsted acids.[13]



Scheme 1. Propargylation of terminal and internal alkynes. OTf = triflate.

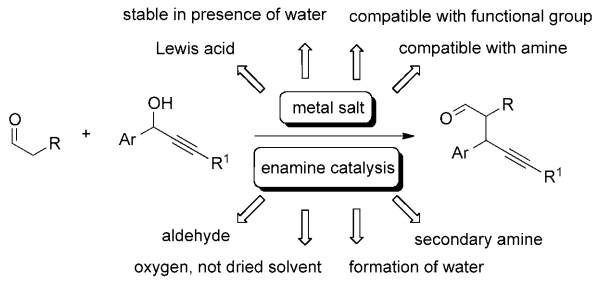
To promote the enantioselective propargylic alkylation of internal alkynes, a metal catalyst needs to be able to act in a cooperative manner[14] with the organocatalyst. Moreover, the metal catalyst needs to have a reduced activity towards the π-activation of alkynes (as in gold-, silver-, or platinum-catalyzed reactions) and it needs to tolerate the presence of secondary amine, aldehydes, and water that are formed during the catalytic cycle (Scheme 2).

Herein, we report a facile, catalytic, and highly stereoselective organocatalytic alkylation of internal propargylic alcohols with aldehydes in the presence of water as the reaction solvent. In addition, the methodology is quite versatile and tolerant towards functional groups and it allows the use of highly functionalized internal alkynes and aldehydes.

Recently, we have focused our attention on the development of α-alkylation of aldehydes by S_N1-type reactions with alcohols.[11a] We found that $InBr_3$, used in catalytic amounts, was able to induce alkylation of allylic alcohols by organocatalysis.[11b] Indium salts were found to be suitable for the formation of less stabilized carbocations, and were not deactivated by aldehydes, secondary amines (MacMillan catalyst),[15] or water, which are present in the reaction mixture. The compatibility of indium with organocatalytic reac-

[a] Dr. R. Sinisi, M. V. Vita, Dr. A. Gualandi, Dr. E. Emer, Prof. P. G. Cozzi
Dipartmento di Chimica "G. Ciamician"
ALMA MATER STUDIORUM, Università di Bologna
Via Selmi 2, 40126 Bologna (Italy)
Fax: (+39) 051-2099456
E-mail: piergiorgio.cozzi@unibo.it

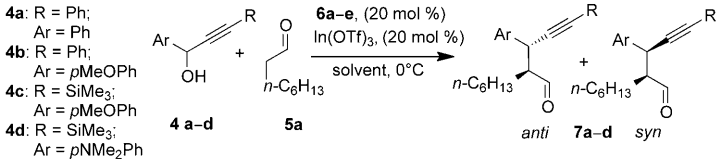
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/chem.201100729.

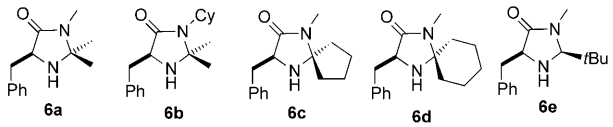


Scheme 2. Favorable combination of cooperative catalysts for the alkylation of internal alkynes.

tions prompted us to explore other stabilized carbocations in the alkylation of internal propargylic alcohols. The alcohols **4a–d** were selected as model substrates and the reaction was performed in the presence of indium salts with the MacMillan catalysts **6a–e**. No reaction occurred if the MacMillan catalysts were used with alcohols and octanal in the absence of indium salts. Even the propargylic alcohol **4d**, which is able to form a stabilized carbocation, was completely unreactive in the absence of indium salts under the reaction conditions employed (Table 1).

Table 1. Organocatalytic α-alkylation of octanal with propargylic alcohols in the presence of indium(III) salts.





Alcohol	Cat.	Solvent	Yield [%]	d.r.[b]	*ee* [%][c]
4c[d,e]	**6e**	CH_2Cl_2	>95	1:1	40/20
4c[d]	**6e**	CH_2Cl_2	>95	1.1:1	63/47
4c[f]	**6c**	H_2O	–	–	–
4d	**6a**	CH_2Cl_2	75	1.1:1	98/94
4d	**6b**	CH_2Cl_2	70	1.2:1	97/97
4d	**6c**	CH_2Cl_2	56	1.3:1	95/90
4d	**6d**	CH_2Cl_2	<10	1:1	n.d.[g]
4d	**6e**	CH_2Cl_2	90	3:1	69/41
4d	**6c**	$CHCl_3$	90	1.3:1	95/84
4d	**6c**	H_2O	95	3.3:1	98/88
4d	**6a**	CH_2Cl_2	75	1.1:1	98/94

[a] Reaction conditions: alcohols **4a–d** (0.1 mmol), octanal **5a** (0.3 mmol), 20% of the catalyst **6a–e**, solvent (0.5 mL), and 20 mol% of the corresponding indium salt (0.33 M solution in CH_3CN) at 0°C for 16–24 h. [b] For all the reactions the d.r. ratio was determined by ^{1}H NMR spectroscopic analysis. The ratio is indicated as *anti* versus *syn*. [c] Determined by chiral HPLC analysis of the isolated products or of the corresponding alcohols. See the Supporting Information for details. [d] Reaction time: 4 h at RT. No reaction occurred in 24 h at 0°C. [e] $InBr_3$ (20 mol%) was used as Lewis acid. [f] No reaction occurred. [g] n.d. = not determined.

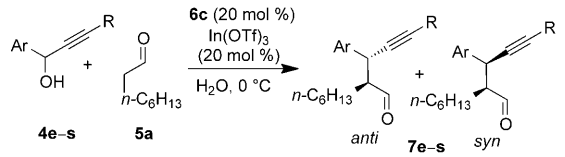
We observed that substrate **4a** was unreactive, whereas **4b** reacted very slowly (more than 40 h). However, **4c** and **4d** in dichloromethane gave the desired products in less than 24 h. The alcohol **4c** was not reactive at 0°C. For both substrates the diastereomeric ratio (d.r.) was quite low when the MacMillan catalysts **6a–d** were employed in the reaction. Catalyst **6e** gave an acceptable d.r. with alcohol **4d** but the enantiomeric excesses recorded were quite low. We found an increased stereoselectivity when undergoing the propargylation in the presence of water.[16] However, under these conditions only substrate **4d** had shown reactivity.[17] In general, the reaction was promoted in the presence of $In(OTf)_3$, whereas other indium salts gave slightly inferior results in terms of diastereoselectivity. Although the MacMillan catalyst **6e** gave a poor stereoselectivity in the reaction, the use of the catalysts **6c**[18] in the presence of water gave a good d.r. and excellent enantiocontrol with alcohol **4d**. It is noteworthy that the use of water as the reaction medium is well-explored in organocatalysis.[19] Although we have not observed a dramatic acceleration of the reaction typical of "on water" conditions,[20] it is quite remarkable that the S_N1 reaction is not hampered by water and that the reaction is working only in the presence of indium salts.

The subtle role played by water in organocatalytic processes was recently highlighted by Wennemers[21] and Flowers,[22] whereas the compatibility of Lewis acid with water in terms of their kinetic stability and water exchange processes was reported by Kobayashi.[23] Indium salts have the desirable characteristic of stability and compatibility to promote acidic processes in the presence of water. Furthermore, the S_N1 type reaction of a propargylic cation in water is dictated by the stability of the carbocation relative to the nucleophilicity of water.[24] Based on the Mayr table[10] we have selected the substrates **4e–s** for exploring the scope of our reaction and the results are illustrated in Tables 2 and 3.

Different substrates (**4e–s**) were obtained from the corresponding aldehydes (see the Supporting Information for details). Aryl, indole, or naphthyl groups attached to the propargylic alcohols did not significantly affect the reactivity or selectivity of the reaction.

Quite remarkably, the reaction tolerates a range of functional groups including thio, amides, silyl ether, and even acetals in the alkyne moiety. The presence of groups that are able to stabilize the carbenium ion is mandatory for the reaction. When other functionalized aldehydes were used with **4d**, the corresponding products were isolated in good yields as a mixture of two diastereoisomers, each one with high stereoselectivity, showing that the reaction has also broad scope with respect to the aldehyde (Table 3). The relative configurations of the *syn* and *anti* products were assigned by comparison with products obtained by Nishibayashi,[9] whereas the absolute configuration was assigned by chemical correlation to a known product (see the Supporting Information for details).[25] The absolute and relative configurations of the products obtained in the reaction are in general agreement with the model that we have suggested

Table 2. Stereoselective propargylation of octanal with MacMillan catalyst in the presence of catalytic amount of $In(OTf)_3$.

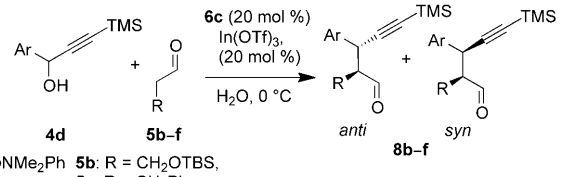


4e: Ar = *p*NMe_2Ph; R = TIPS
4f: Ar = *p*NMe_2Ph, R = TBS
4g: Ar = *p*NMe_2Ph, R = TPS
4h: Ar = *p*NMe_2Ph, R = *n*-C_4H_9
4i: Ar = *p*NMe_2Ph, R = $CH(OEt)_2$
4j: Ar = *p*NMe_2Ph, R = CH_2CH_2Ph
4k: Ar = *p*NMe_2Ph, R = CH_2N(BOC)Ph
4l: Ar = *p*NMe_2Ph, R = CH_2CH_2OTHP
4m: Ar = *p*NMe_2Ph, R = CH_2CH_2OTBS
4n: Ar = *p*NMe_2Ph, R = CH_2SPh
4o: Ar = 2-Cl-4-NMe_2Ph, R = TMS
4p: Ar = 2-Me-4-NMe_2Ph, R = TMS
4q: Ar = 4-NMe_2-1-Napthyl, R = TMS
4r: Ar = (*N*-TIPS)-2-Indolyl, R = TMS
4s: Ar = (*N*-Me)-2-Indolyl, R = TMS

Entry[a]	Product	Yield [%][b]	d.r.[c]	*ee* [%] *anti*[d]	*ee* [%] *syn*[d]
1	**7e**	87	3.0:1	92	87
2	**7f**	70	2.6:1	96	91
3	**7g**	87	3.0:1	96	92
4	**7h**	92	3.0:1	98	94
5	**7i**	97	2.6:1	97	94
6	**7j**	91	2.5:1	96	91
7	**7k**	80	3.0:1	97	98
8	**7l**	93	2.1:1	94	90
9	**7m**	94	2.5:1	98	92
10	**7n**	96	2.6:1	92	92
11	**7o**	84	4.9:1	99	96
12	**7p**	95	4.4:1	96	95
13	**7q**	71	6.7:1	93	86
14	**7r**	86	1.3:1	92	72
15	**7s**	98	1:1.4[e]	95	94

[a] The reactions were performed at 0 °C with alcohol **4e–s** (1 equiv), octanal **5a** (3 equiv), in the presence of catalyst **6c** (20 mol %). $In(OTf)_3$ (20 mol %, 0.33 M solution in CH_3CN) was added to the reaction mixture containing the aldehyde, the alcohol **4e–s** and the catalyst **6c**, and the reactions were run until completion, shown by TLC (16–24 h). TIPS = triisopropylsilyl, TBS = *tert*-butyldimethylsilyl, TPS = triphenylsilyl, BOC = *tert*-butoxycarbonyl, THP = tetrahydropyran-2-yl. [b] Yield after chromatographic purification. [c] For all the reactions the d.r. (*anti* vs. *syn*) was measured by using ^{1}H NMR and HPLC analyses. [d] Determined by chiral HPLC analysis of the isolated products or of the corresponding alcohols. See the Supporting Information for details. [e] The major diasteroisomer in this case was the *syn* one.

Table 3. Organocatalytic alkylation of functionalized aldehydes **5b–f** with the propargylic alcohol **4d**.



Ar = *p*NMe_2Ph **5b**: R = CH_2OTBS,
5c: R = CH_2Ph,
5d: R = CH_2NHBOC,
5e: R = CH_2NHTs,
5f: R = $CH_2CH_2CH_2Cl$,

Entry[a]	Product	Yield [%][b]	d.r.[c]	*ee* [%] *anti*[d]	*ee* [%] *syn*[d]
1	**8b**	64	3.3:1	91	99
2	**8c**	95	1.8:1	94	90
3	**8d**	97	3.0:1	93	86
4	**8e**	87	1.9:1	91	75
6	**8f**	90	2.5:1	94	93

[a] The reactions were performed at 0 °C with alcohol **4d** (1 equiv), aldehyde **5b–f** (3 equiv), in the presence of catalyst **6c** (20 mol %). $In(OTf)_3$ (20 mol %, 0.33 M solution in CH_3CN) was added to the reaction mixture containing the aldehyde, alcohol **4d**, catalyst **6c**, and the reactions were run until completion by TLC (16–24 h). [b] Yield after chromatographic purification. [c] For all the reactions the d.r. (*anti* vs. *syn*) was measured by using ^{1}H NMR and HPLC analyses. [d] Determined by chiral HPLC analysis of the isolated products or of corresponding alcohols. See the Supporting Information for details.

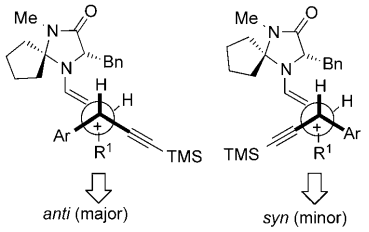


Figure 1. Proposed transition state stereochemical models for enantioselective propargylations.

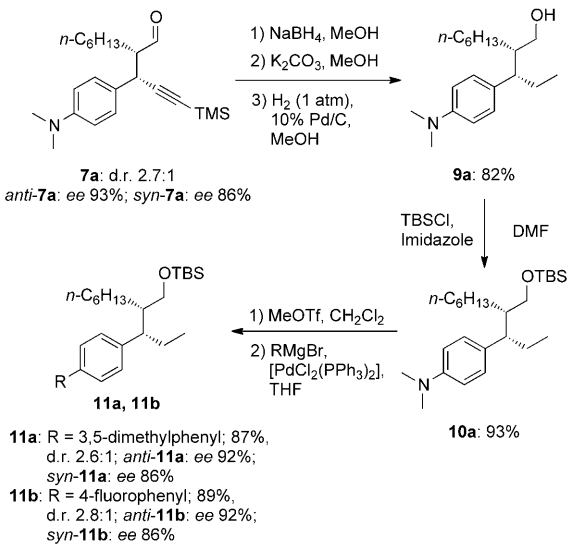
for the alkylation of aldehydes with alcohols using the MacMillan catalyst (Figure 1).[11a,b]

The presence of the dimethylamino functionality as an activating group for substrates towards the addition of aldehydes can be advantageously used in further useful transformations, thereby enhancing the scope of our chemistry. Recently, MacMillan and co-workers[26] and Senanayake and co-workers,[27] have described the nickel- and palladium-catalyzed substitution of the dimethylamino group. This strategy was used by MacMillan in the context of a total synthesis.[28]

The substrate **10a** (obtained from **7a** by reduction with $NaBH_4$, removal of the silyl group, catalytic hydrogenation of the triple bond and successive protection with *t*BuMe_2SiCl) was transformed into the corresponding ammonium triflate by treatment with methyl triflate. Subsequent treatment of the ammonium salt with 3,5-Me_2PhMgBr and 4-FPhMgBr in the presence of catalytic amounts of the palladium complex $[PdCl_2(Ph_3P)_2]$ gave the desired product **11a** or **11b**, respectively, in good yields with no racemization, showing the possibility to further functionalize the product obtained in our reaction.

Our results are complementary to those obtained by Nishibayashi,[9,12] in which the major *syn* diastereoisomer was isolated (up to 3.3:1). It is noteworthy that adducts obtained by the methodology described by Nishibayashi are also accessible through our method, by a straightforward desilylation with K_2CO_3/MeOH (e.g., Scheme 3, the transformation of **7a** into **9a**).

In conclusion, we have described the first catalytic stereoselective addition of aldehydes to internal functionalized propargylic alcohols, promoted by a combination of an organocatalyst and indium triflate. The reaction is tolerant of a range of functional groups and was performed in the presence of water. The possibility to induce the formation of carbenium ion in the presence of water by merging an organo-



Scheme 3. Functionalization of the products obtained by the organocatalytic alkylation through a Pd-catalyzed arylation of the trimethylammonium triflate.

catalytic process with a Lewis acid[29] opens up several new opportunities in the area of organocatalysis.[30]

Experimental Section

General procedure: The compounds **4c–s** (0.1 mmol, 1 equiv) and aldehyde (0.3 mmol, 3 equiv) were added to a vial containing the MacMillan catalyst **6c** (0.02 mmol, 20 mol%) in H_2O (0.5 mL) at 0°C. The mixture was stirred for 1 min and at the same temperature a solution of $In(OTf)_3$ (20 mol%, 0.33 M in acetonitrile) was slowly added. The mixture was stirred for 24 h at the same temperature and was then diluted with Et_2O. The organic layer was separated and the aqueous layer was extracted twice with Et_2O. The collected organic layers were dried over Na_2SO_4 and then concentrated. The residue was purified by flash chromatography.

Acknowledgements

PRIN (Progetto Nazionale Stereoselezioni in Chimica Organica: Metodologie ed Applicazioni), Bologna University, Fondazione Del Monte, and the European Commission through the project FP7-201431 (CATAFLU.OR) are acknowledged for financial support.

Keywords: aldehydes · enamine · indium · organocatalysis · propargylation

[1] For reviews, see: a) P. Melchiorre, M. Marigo, A. Carlone, G. Bartoli, *Angew. Chem.* **2008**, *120*, 6232–6265; *Angew. Chem. Int. Ed.* **2008**, *47*, 6138–6171; b) C. F. Barbas III, *Angew. Chem.* **2008**, *120*, 44–50; *Angew. Chem. Int. Ed.* **2008**, *47*, 42–47; c) G. Lelais, D. W. C. MacMillan, *Aldrichimica Acta* **2006**, *39*, 79–87. For a recent overview, see: D. W. C. MacMillan, *Nature* **2008**, *455*, 304–308.

[2] a) S. B. Jones, B. Simmons, D. W. C . MacMillan, *J. Am. Chem. Soc.* **2009**, *131*, 13306–13307; b) J. Carpenter, A. B. Northrup, D. M. Chung, J. J. M. Wieners, S.-G. Kim, D. W. C. MacMillan, *Angew. Chem.* **2008**, *120*, 3624–3628; *Angew. Chem. Int. Ed.* **2008**, *47*, 3568–3572; c) R. M. Wilson, W. S. Jen, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2005**, *127*, 11616–11617.

[3] J. E. Wilson, A. D. Casarez, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2009**, *131*, 11332–11334.

[4] S. Mukherjee, J. W. Yang, S. Hodffmann, B. List, *Chem. Rev.* **2007**, *107*, 5471–5569.

[5] A. Errkilä, I. Majander, P. M. Pihko, *Chem. Rev.* **2007**, *107*, 5416–5470.

[6] a) T. D. Beeson, A. Mastracchio, J. Hong, K. Ashton, D. W. C. MacMillan, *Science* **2007**, *316*, 582–585; b) F. Benfatti, M. Guiteras Capdevila, L. Zoli, E. Benedetto, P. G. Cozzi, *Chem. Commun.* **2009**, 469–470.

[7] D. Nicewicz, D. W. C. MacMillan, *Science* **2008**, *322*, 77–80.

[8] Z. ShaoHashmi, H. Zhang, *Chem. Soc. Rev.* **2009**, *38*, 2745–2755. For a combination of gold and organocatalysis, see: S. Belot, K. A. Vogt, C. Besnard, N. Krause, A. Alexakis, *Angew. Chem.* **2009**, *121*, 9085–9088; *Angew. Chem. Int. Ed.* **2009**, *48*, 8923–8926. For an overview, see: A. S. Hashmi, C. Hubbert, *Angew. Chem.* **2010**, *122*, 1026–1028; *Angew. Chem. Int. Ed.* **2010**, *49*, 1010–1012.

[9] M. Ikeda, Y. Miyake, Y. Nishibayashi, *Angew. Chem.* **2010**, *122*, 7295–7295; *Angew. Chem. Int. Ed.* **2010**, *49*, 7139–7139.

[10] Stability and reactivity of carbenium ions are described by careful analysis of Mayr, see: H. Mayr, B. Kempf, A. R. Ofial, *Acc. Chem. Res.* **2003**, *36*, 66–77, and ref. therein.

[11] For a highlight, see: P. G. Cozzi, F. Benfatti, *Angew. Chem.* **2010**, *122*, 264–267; *Angew. Chem. Int. Ed.* **2010**, *49*, 256–259. For the use of alcohols in S_N1-type organocatalytic reactions, see: a) P. G. Cozzi, F. Benfatti, L. Zoli, *Angew. Chem.* **2009**, *121*, 1339–1342; *Angew. Chem. Int. Ed.* **2009**, *48*, 1313–1316; b) M. Guiteras Capdevila, F. Benfatti, L. Zoli, M. Stenta, P. G. Cozzi, *Chem. Eur. J.* **2010**, *16*, 11237–11241; c) L. Zhang, L. Cui, X. Li, S. Luo, J.-P. Cheng, *Chem. Eur. J.* **2010**, *16*, 2045–2049; d) G. Bergonzini, S. Vera, P. Melchiorre, *Angew. Chem.* **2010**, *122*, 9879–9882; *Angew. Chem. Int. Ed.* **2010**, *49*, 9685–9688.

[12] Similarly, the enantioselective propargylic alkylation of propargylic esters in the presence of the Hayashi–Jørgensen catalyst occurred through a copper–allenylidene complex, see: A. Yoshida, M. Ikeda, G. Hattori, Y. Miyake, Y. Nishibayashi, *Org. Lett.* **2011**, *13*, 592–595. The copper-catalyzed enantioselective alkylation of propargyl acetate working with a similar mechanism was reported, see: P. Fang, X.-L. Hou, *Org. Lett.* **2009**, *11*, 4612–4615. Also in this case no reaction was reported with internal alkynyl acetates.

[13] For a review, see: E. Emer, R. Sinisi, D. Petruzziello, F. De Vincetiis, P. G. Cozzi, *Eur. J. Org. Chem.* **2011**, 647–666.

[14] For example of cooperative catalytic systems, see: a) thiourea and Brønsted acids: H. Xu, S. J. Zuend, M. G. Woll, Y. Tao, E. N. Jacobsen, *Science* **2010**, *327*, 986–990; b) carbene and Lewis acids: B. Cardinal-David, D. E. A. Raup, K. A. Scheidt, *J. Am. Chem. Soc.* **2010**, *132*, 5345–5347; c) carbene and aminocatalysis: S. T. Lathrop, T. Rovis, *J. Am. Chem. Soc.* **2009**, *131*, 13628–13630.

[15] S. G. Ouellet, A. Walij, D. W. C. MacMillan, *Acc. Chem. Res.* **2007**, *40*, 1327–1339.

[16] At the present time we have no conclusive explanation for this remarkable behavior. As the d.r. of the reaction is determined by the approach of the carbenium ion to the chiral enamine (Scheme 2), subtle sterical and solvent effects could be involved. High level DFT calculations are in progress.

[17] When water is the reaction solvent, the most reactive carbocation formed by **4a–c** is rapidly intercepted by water, and thus, the reaction does not occur.

[18] T. J. Peelen, Y. G. Chi, S. H. Gellman, *J. Am. Chem. Soc.* **2005**, *127*, 11598–11599.

[19] N. Mase, C. F. Barbas, *Org. Biomol. Chem.* **2010**, *8*, 4043–4050.

[20] S. Narayan, J. Muldoon, M. G. Finn, W. Fokin, H. C. Kolb, K. B. Sharpless, *Angew. Chem.* **2005**, *117*, 3339–3343; *Angew. Chem. Int. Ed.* **2005**, *44*, 3275–3279.
[21] M. Wiesner, G. Upert, G. Angelici, H. Wennemers, *J. Am. Chem. Soc.* **2010**, *132*, 6–7.
[22] J. J. Devery, J. C. Conrad, D. W. C. MacMillan, R. A. Flowers, *Angew. Chem.* **2010**, *122*, 6242–6246; *Angew. Chem. Int. Ed.* **2010**, *49*, 6106–6110.
[23] H. Yamamoto, S. Kobayashi, *Synlett* **2008**, 1537–1542.
[24] T. B. Phan, M. Breugst, H. Mayr, *Angew. Chem.* **2006**, *118*, 3954–3959; *Angew. Chem. Int. Ed.* **2006**, *45*, 3869–3874.
[25] Propanal was alkylated with the alcohol **4s**. The product was reduced with $NaBH_4$, then desilylated and hydrogenated with Pd/C. The same product was obtained by the Michael addition of *N*-methylindole to (*E*)-pent-2-enal, promoted in a stereoselective manner by a catalytic amount of 9-amino(9-deoxy)*epi*-hydroquinine, see: P. Galzerano, F. Pesciaioli, A. Mazzanti, G. Bartoli, P. Melchiorre, *Angew. Chem.* **2009**, *121*, 8032–8034; *Angew. Chem. Int. Ed.* **2009**, *48*, 7892–7894.
[26] S. B. Blakey, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2003**, *125*, 6046–6047.
[27] J. T. Reeves, D. R. Fandrick, Z. Tan, J. J. Song, H. Lee, N. K. Jee, C. H. Senanayake, *Org. Lett.* **2010**, *12*, 4388–4391.
[28] N. Paras, B. Simmons, D. W. C. MacMillan, *Tetrahedron* **2009**, *65*, 3232–3238.
[29] A. E. Allen, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2010**, *132*, 4986–4987.
[30] When this work was submitted for publication, Nishibayashi published a cooperative catalytic reaction using indium(III) and the MacMillan catalyst, see: K. Motoyama, M. Ikeda, Y. Miyake, Y. Nishibayashi, *Eur. J. Org. Chem.* **2011**, 2239–2246. Using our findings reported in reference [11b] and with CH_2Cl_2 as the reaction solvent; they achieved good enantiomeric excesses for propargylic alcohols with *para* and *ortho* methoxy groups, with a poor d.r. (1.0:1.1).

Received: March 9, 2011
Published online: May 26, 2011

